



# Leisure-Time Running Reduces the Risk of Incident Type 2 Diabetes

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## ABSTRACT

**OBJECTIVES:** We examined the overall association as well as the dose–response relationship between leisure-time running and incident type 2 diabetes.

**METHODS:** Participants were 19,347 adults aged 18–100 years who were free of cardiovascular disease, cancer, and diabetes at baseline, and who received at least 2 extensive preventive medical examinations between 1974 and 2006. Running and other types of aerobic physical activity were assessed by self-reported leisure-time activities. Type 2 diabetes was defined as fasting glucose  $\geq 126$  mg/dL (7.0 mmol/L), physician diagnosis, or insulin use.

**RESULTS:** During an average follow-up of 6.5 years, 1015 adults developed type 2 diabetes. Approximately 29.5% of adults participated in leisure-time running at baseline. Runners had a 28% (hazard ratio [HR] 0.72; 95% confidence interval [CI], 0.62–0.84) lower risk of developing type 2 diabetes compared with nonrunners during follow-up. The HRs (95% CIs) of type 2 diabetes were 0.98 (0.75–1.28), 0.69 (0.51–0.92), 0.62 (0.45–0.85), 0.78 (0.59–1.04), and 0.57 (0.42–0.79) across quintiles of running time (minutes/week) compared with nonrunners after adjusting for potential confounders, including levels of nonrunning aerobic physical activity. Similar dose–response relationships between running distance (miles/week), frequency (times/week), total amount (MET-minutes/week), and speed (mph) were also observed.

**CONCLUSIONS:** Participating in leisure-time running is associated with a lower risk of developing type 2 diabetes in adults. Consistent linear dose–response relationships were observed between various running parameters and incident type 2 diabetes, supporting the prescription of running to prevent type 2 diabetes.

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**KEYWORDS:** Aerobic exercise; Cohort; Running; Type 2 diabetes

## INTRODUCTION

The global prevalence of type 2 diabetes, which is an established risk factor for cardiovascular diseases,<sup>1</sup> has increased

drastically over the past decade. Diabetes is projected to have an even greater growth over coming years in the United States, increasing to more than 54.9 million patients in 2030.<sup>2</sup>

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**Authorship:** DCL had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. DCL, YW, and AGB developed the study concept and design, performed the statistical analyses, and drafted the manuscript.

SNB, XS, and DCL obtained the funding and supervised the study. XS and DCL provided the administrative, technical, or material support. YW, DCL, AGB, TMHE, XS, TSC, CJL, and SNB contributed to the final manuscript.

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Type 2 diabetes develops as a result of genetics and environmental factors, including modifiable risk factors.<sup>3</sup> Among these lifestyle behaviors, regular physical activity has been regarded as one of the key elements to lower the risk of type 2 diabetes and delay its onset.<sup>4,5</sup>

While the benefits of moderate-intensity physical activity (defined as any physical activity requiring an energy expenditure of  $\geq 3$ -6 metabolic equivalent [MET]<sup>6</sup>) on the primary prevention of type 2 diabetes is well established,<sup>7</sup> fewer studies focus on the protective effect of vigorous-intensity physical activity ( $\geq 6$  METs). Mounting evidence suggests that vigorous-intensity physical activity improves cardiorespiratory fitness, which is inversely associated with the incidence of type 2 diabetes,<sup>8</sup> more effectively than moderate-intensity physical activity.<sup>9,10</sup> Moreover, vigorous-intensity physical activity has been shown to attenuate weight gain more adequately than moderate-intensity physical activity,<sup>11</sup> which is related to a higher risk of type 2 diabetes.<sup>12</sup> Therefore, vigorous-intensity physical activity, such as running, may confer superior benefits over other types of physical activity on preventing type 2 diabetes.

Of the different types of exercise, running is the most popular among individuals who do participate in vigorous-intensity physical activity.<sup>13</sup> Running is convenient and easily accessible, because it does not require specialized equipment or locations. Additionally, running is usually well above the MET level of 6,<sup>14</sup> and even slow jogging is considered as vigorous-intensity physical activity.<sup>15</sup> Current public health physical activity guidelines recommend that individuals should perform at least 500 MET-min/week of physical activity (equivalent to at least 75 minutes/week of vigorous-intensity physical activity) to obtain general health benefits, including type 2 diabetes prevention.<sup>16</sup> Because the primary barrier preventing people from exercising is lack of time,<sup>17</sup> performing vigorous-intensity physical activity, such as running, may motivate more people to achieve the recommended levels of physical activity.

The objective of this study was to examine the association of leisure-time running and type 2 diabetes incidence after adjusting for potential confounders, including other types of aerobic physical activity. Furthermore, the dose-response relationships of various leisure-time running parameters—such as running time, distance, frequency, total amount, and speed—with the risk of type 2 diabetes were investigated.

## MATERIAL AND METHODS

### Study Population

We analyzed data from the Aerobics Center Longitudinal Study (ACLS), which is a prospective cohort study

designed to examine the associations of clinical and lifestyle factors with health outcomes. Participants were predominantly non-Hispanic white individuals who were well educated and belonged to middle-to-upper socioeconomic strata.<sup>18</sup> The 21,350 participants aged 18-100 years received at least 2 extensive medical examinations at the Cooper Clinic in Dallas, Texas, between 1974 and 2006.

Participants were excluded if they reported a history of myocardial infarction, stroke, or cancer ( $n = 1005$ ), or had diabetes ( $n = 998$ ) at baseline. This resulted in a final study sample of 19,347 men and women for the analyses. The Cooper Institute Institutional Review Board approved the study protocol annually, and all participants gave their written informed consent prior to data collection at baseline and during follow-up examinations. Further details of the ACLS design, sampling procedures, and data collection have been previously described.<sup>18,19</sup>

### CLINICAL SIGNIFICANCE

- Participating in leisure-time running is associated with a lower risk of developing type 2 diabetes in adults.
- Consistent linear dose-response relationships were observed between various running parameters and incident type 2 diabetes.
- We noted significant benefits of running with lower doses and intensities supporting the prescription of running to prevent type 2 diabetes in adults, in addition to other healthy lifestyle behaviors.

### Clinical Examination

After a 12-hour overnight fast, participants underwent comprehensive medical examinations at baseline, which included body weight and height assessments, blood chemistry analyses, electrocardiography, physical examination, and a detailed medical history questionnaire. In addition, a maximal treadmill exercise test was performed to assess cardiorespiratory fitness. Smoking status, alcohol consumption, personal history of hypertension, hypercholesterolemia, myocardial infarction, stroke, cancer, diabetes, and parental history of diabetes were assessed by standardized medical history questionnaires.

### Assessment of Running

Physical activity information for the preceding 3 months was collected from the physical activity questionnaire. Participants were asked to fill in 4 questions about their running or jogging habits that addressed the duration, distance, frequency, and speed. Based on the information from the physical activity questionnaire, total weekly running time was calculated by multiplying the average duration of running and the frequency. Total amount of running was calculated by multiplying the MET value for the given speed and the weekly running time.<sup>20</sup> Runners in this study were defined as those who reported running in all 4 questions under the running section. Participants were classified into 6 groups: nonrunners and 5 quintiles of weekly running time (minutes), distance (miles), frequency (times), total amount (MET-minutes), and speed (mph) in runners, following our previous study methods.<sup>21</sup> Total amount of other

nonrunning aerobic physical activity (eg, walking, cycling, swimming, aerobic dance, racquetball, skating, and other sports-related activities) was calculated and classified into 3 groups: 0, 1-499, and  $\geq 500$  MET-minutes per week based on the physical activity guidelines. Details of the physical activity assessment have been previously described.<sup>22</sup>

### Ascertainment of Type 2 Diabetes

The diagnosis of type 2 diabetes was determined at a follow-up examination according to the American Diabetes Association criteria, which defines type 2 diabetes as a fasting plasma glucose concentration  $\geq 126$  mg/dL ( $\geq 7.0$  mmol/L),<sup>23</sup> physician diagnosis, or use of insulin. Follow-up time was calculated from the baseline examination to the first event of type 2 diabetes or the last follow-up observation through 2006 for participants who did not develop type 2 diabetes.

### Statistical Analysis

Baseline characteristics of participants were summarized using descriptive statistics by quintiles of weekly running time. Cox proportional hazard regression was used to compute hazard ratios (HRs) and 95% confidence intervals (CIs) of type 2 diabetes according to exposure categories. Participants who reported no running activity were the reference group. The potential effect modification by sex on

the association between running and type 2 diabetes incidence was examined using interaction terms in the Cox regression and by comparing risk estimates in the sex-stratified analyses. Because no significant interaction was found ( $P = .10$ ), the pooled analyses were conducted. The proportional hazards assumption was tested and satisfied by comparing the log-log survival plots.

To determine whether the association between running status (runners vs nonrunners) and incident type 2 diabetes varied by lifestyle factors or health conditions, the interactions of these dichotomized baseline characteristics were tested in the Cox regression.

SAS version 9.4 (SAS Institute, Cary, NC) was used for all analyses. Two-sided tests were used, and a  $P$  value  $< .05$  was considered statistically significant.

### RESULTS

After an average follow-up of  $6.5 \pm 6.1$  years (minimum, 0.1 year; maximum, 31.8 years), 1015 (5.3%) of the 19,347 participants developed type 2 diabetes. Among our sample, approximately 29.5% performed leisure-time running ( $n = 5707$ ) at baseline (Table 1). Compared with nonrunners, runners were more likely to be younger, male, leaner, non-smokers, heavy alcohol drinkers, less active in other types of aerobic physical activity, had lower prevalence of chronic diseases (hypertension, hypercholesterolemia, and

**Table 1** Baseline Characteristics of Participants in the Aerobics Center Longitudinal Study, 1974-2006, by Quintile of Weekly Running Time

Characteristics	Quintile of Weekly Running Time (Minutes/Week)							P Value
	All N = 19,347	Nonrunners (0) n = 13,640	Q1 (<51) n = 1141	Q2 (51-80) n = 1186	Q3 (81-116) n = 1111	Q4 (117-174) n = 1133	Q5 ( $\geq 175$ ) n = 1136	
Age (years)	44.1 (9.6)	45.0 (9.8)	40.9 (8.7)	41.6 (8.8)	42.0 (8.4)	42.8 (8.6)	43.1 (8.9)	< .001
Sex (male)	15648 (80.9)	10578 (77.6)	1036 (90.8)	1055 (89.0)	995 (89.6)	996 (87.9)	988 (87.0)	< .001
BMI (kg/m <sup>2</sup> )	25.6 (3.8)	25.9 (4.0)	25.3 (2.9)	25.0 (3.1)	24.8 (3.0)	24.8 (3.0)	24.1 (2.7)	< .001
Current smokers	2863 (14.8)	2287 (16.8)	136 (11.9)	145 (12.2)	112 (10.1)	91 (8.0)	92 (8.1)	< .001
Heavy alcohol drinking	3451 (17.8)	2376 (17.4)	237 (20.8)	202 (17.0)	209 (18.8)	200 (17.7)	227 (20.0)	.022
Nonrunning aerobic physical activity (MET-min/week)								
0	12,241 (63.3)	8019 (58.8)	762 (66.8)	856 (72.2)	848 (76.3)	879 (77.6)	877 (77.2)	< .001
1-499	2710 (14.0)	2282 (16.7)	106 (9.3)	111 (9.3)	73 (6.6)	81 (7.1)	57 (5.0)	
$\geq 500$	4396 (22.7)	3339 (24.5)	273 (23.9)	219 (18.5)	190 (17.1)	173 (15.3)	202 (17.8)	
Systolic blood pressure (mm Hg)	120 (14)	120 (14)	119 (13)	119 (13)	119 (14)	120 (13)	120 (14)	.014
Diastolic blood pressure (mm Hg)	80 (10)	80 (10)	79 (9)	79 (10)	79 (9)	79 (9)	79 (9)	< .001
Hypertension	5337 (27.6)	4007 (29.4)	229 (20.1)	275 (23.2)	265 (23.9)	284 (25.1)	277 (24.4)	< .001
Total cholesterol (mg/dL)	206.2 (38.7)	208.0 (39.2)	201.4 (36.7)	202.4 (38.6)	203.5 (36.2)	201.7 (37.3)	200.5 (37.9)	< .001
Hypercholesterolemia	4980 (25.7)	3797 (27.8)	241 (21.1)	246 (20.7)	223 (20.1)	249 (22.0)	224 (19.7)	< .001
Abnormal ECG	1318 (6.8)	1056 (7.7)	56 (4.9)	51 (4.3)	55 (5.0)	49 (4.3)	51 (4.5)	< .001
Parental history of diabetes	1308 (6.8)	1020 (7.5)	67 (5.9)	54 (4.6)	50 (4.5)	62 (5.5)	55 (4.8)	< .001
Cardiorespiratory fitness (METs)	11.4 (2.5)	10.6 (2.1)	12.6 (1.8)	12.9 (1.9)	13.3 (1.9)	13.6 (2.1)	14.7 (2.5)	< .001
Impaired fasting glucose	7618 (39.4)	5482 (40.2)	441 (38.7)	452 (38.1)	410 (36.9)	411 (36.3)	422 (37.2)	.012
Baseline fasting glucose (mg/dL)	97.4 (9.5)	97.6 (9.6)	97.4 (8.9)	97.2 (9.0)	97.0 (9.1)	96.9 (9.0)	96.7 (9.2)	.005

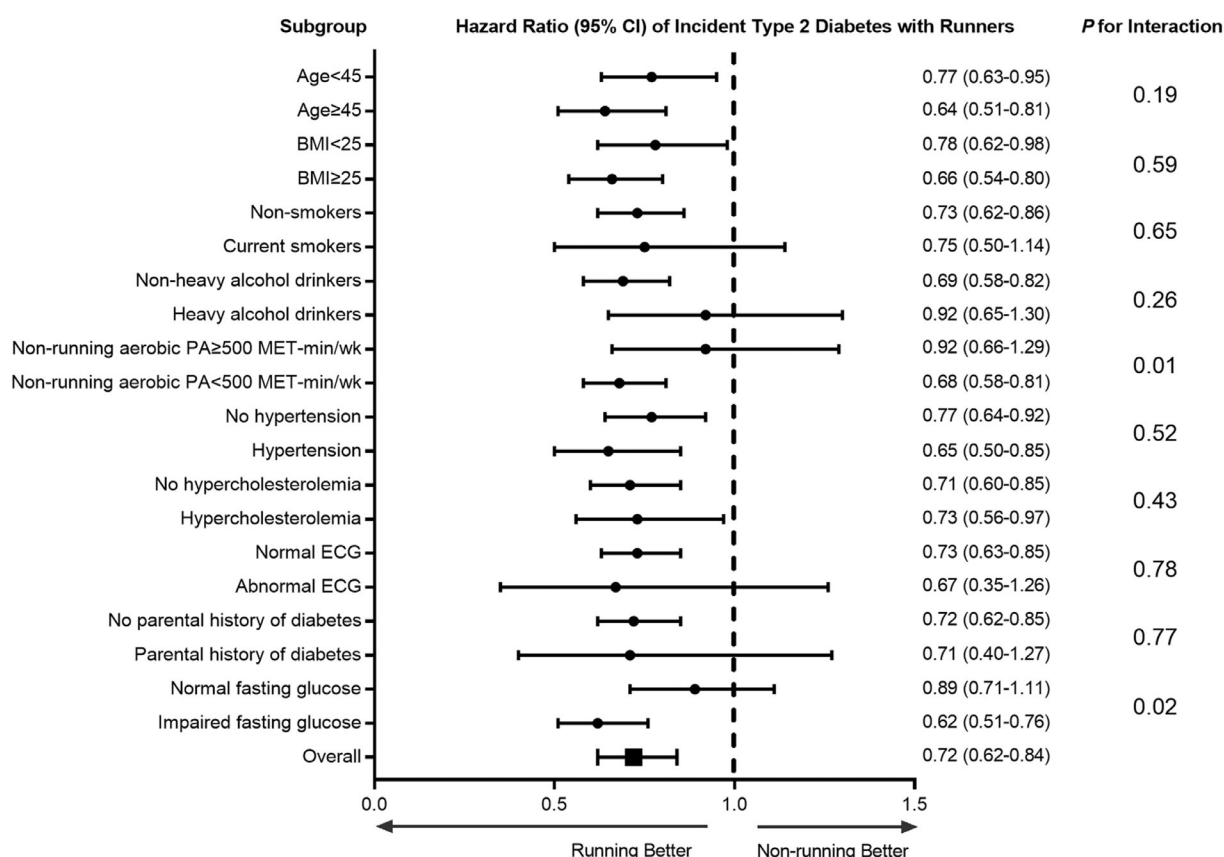
BMI = body mass index; ECG = electrocardiogram; MET = metabolic equivalent.

Data are presented in mean (SD) unless indicated as number (%). Smoking status (never, former, or current), heavy alcohol drinking (defined as average intake of  $> 7$  drinks per week for women, and  $> 14$  drinks per week for men); hypertension (defined by blood pressure  $\geq 140/90$  mm Hg or physician-diagnosed hypertension), and hypercholesterolemia (defined by total cholesterol  $\geq 240$  mg/dL or physician-diagnosed hypercholesterolemia); parental history of diabetes (yes or no); and impaired fasting glucose (defined by an elevated fasting plasma glucose concentration  $\geq 100$  and  $< 126$  mg/dL).

abnormal electrocardiogram), had less parental history of diabetes, and lower baseline fasting glucose (all  $P < .05$ ). Also, runners had higher cardiorespiratory fitness levels than nonrunners ( $P < .001$ ).

Runners had a 28% (HR 0.72; 95% CI, 0.62-0.84) reduced risk of type 2 diabetes compared with nonrunners after adjustment for potential confounders (Figure 1). Stratified analyses examining the effect modifications by baseline characteristics on the association between running status (runners vs nonrunners) and incident type 2 diabetes were conducted (Figure 1). We found no significant interactions in all subgroup analyses except nonrunning aerobic physical activity and impaired fasting glucose (both  $P < .05$ ), indicating that the associations between running status and incident type 2 diabetes were consistent regardless of age, body mass index (BMI), smoking status, heavy alcohol drinking, personal history of hypertension and hypercholesterolemia, electrocardiogram abnormality, and parental history of diabetes.

The dose-response associations between weekly running time and the incidence of type 2 diabetes are provided in Table 2. The group with the highest weekly running time (Quintile 5:  $\geq 175$  minutes/week) had a 52% (HR 0.48; 95% CI, 0.35-0.66) lower risk of developing type 2 diabetes than nonrunners after adjusting for baseline age, sex, and examination year (Model 1). Similar results were found after additional adjustment for baseline smoking status, heavy alcohol drinking, and levels of nonrunning aerobic physical activity (Model 2). Further adjustment for potential mediating factors and confounders, such as baseline BMI, medical conditions, parental history of diabetes, and baseline fasting glucose level attenuated the association, although results were still significant in most running time categories (Model 3). An inverse association between weekly running time and the risk of incident type 2 diabetes was observed in all 3 models (all  $P < .001$ ). When we excluded the participants who reported any nonrunning aerobic physical activity ( $n = 7106$ ) to focus only on the



**Figure 1** Hazard ratios of incident type 2 diabetes by running status in subgroups. The reference group for all subgroup analyses was nonrunners. All hazard ratios were adjusted for age (not in age-stratified analyses), sex, examination year, BMI (not in BMI-stratified analyses), smoking status (not in smoking-stratified analyses), heavy alcohol drinking (not in drinking-stratified analyses), nonrunning aerobic physical activity (not in nonrunning aerobic physical activity meeting the aerobic guidelines-stratified analyses), personal history of hypertension (not in hypertension-stratified analyses), personal history of hypercholesterolemia (not in hypercholesterolemia-stratified analyses), ECG abnormality (not in ECG-stratified analyses), parental history of diabetes (not in diabetes history-stratified analyses), and baseline fasting glucose (not in impaired fasting glucose-stratified analyses). The  $P$ -values for the interactions between running status and dichotomized baseline characteristics are depicted on the right.

BMI = body mass index; CI = confidence interval; ECG = electrocardiogram; MET = metabolic equivalent.



**Table 2** Hazard Ratios of Incident Type 2 Diabetes by Quintile of Weekly Running Time

	Nonrunners (0)	Quintile of Weekly Running Time (Minutes/Week)					P for Linear Trend
		Q1 (<51)	Q2 (51-80)	Q3 (81-116)	Q4 (117-174)	Q5 (≥175)	
No. of participants	13,640	1141	1186	1111	1133	1136	
No. of cases	776	59	47	42	51	40	
Adjusted hazard ratio							
Model 1*	1.00 [reference]	0.86 (0.66-1.12)	0.60 (0.45-0.81)	0.55 (0.40-0.75)	0.68 (0.51-0.90)	0.48 (0.35-0.66)	< .001
Model 2†	1.00 [reference]	0.86 (0.66-1.12)	0.60 (0.45-0.81)	0.55 (0.40-0.75)	0.67 (0.50-0.89)	0.48 (0.35-0.66)	< .001
Model 3‡	1.00 [reference]	0.98 (0.75-1.28)	0.69 (0.51-0.92)	0.62 (0.45-0.85)	0.78 (0.59-1.04)	0.57 (0.42-0.79)	< .001

BMI = body mass index; ECG = electrocardiogram; MET = metabolic equivalent.

\*Model 1 was adjusted for baseline age (years), sex, and examination year.

†Model 2 was adjusted for model 1 plus smoking status (never, former, or current), heavy alcohol drinking (average intake of > 7 drinks per week for women, and > 14 drinks per week for men), and levels of other nonrunning aerobic physical activity (0, 1-499, or ≥ 500 MET-minutes per week).

‡Model 3 was adjusted for Model 2 plus baseline BMI (kg/m<sup>2</sup>), hypertension, hypercholesterolemia, abnormal ECG, parental history of diabetes, and baseline glucose level.

running activity, similar associations were observed with the HRs (95% CIs) of 0.77 (0.54-1.10), 0.57 (0.40-0.82), 0.53 (0.37-0.77), 0.66 (0.47-0.93), and 0.58 (0.41-0.84) across quintiles of running time.

In addition to weekly running time, other running parameters were also associated with a lower risk of type 2 diabetes compared with nonrunners (Figure 2). Weekly running distances ≥ 6 miles (Quintile 2), frequency of ≥ 3 times (Quintile 2), total amount ≥ 540 MET-min (Quintile 2), and speed ≥ 6.7 mph (Quintile 3) had significantly lower risks of type 2 diabetes incidence compared with nonrunners.

The combined effects of running speed (cut point at median value of 6.7 mph) and weekly running distance (cut point at median value of 10 miles) on the risk of type 2 diabetes were examined. Compared with nonrunners, the lowest risk of type 2 diabetes was found in the group with faster speed (≥ 6.7 mph) and longer weekly distance (≥ 10 miles) with the HR (95% CI) of 0.58 (0.46-0.74), followed by the faster speed (≥ 6.7 mph) and shorter distance (< 10 miles) group: 0.73 (0.55-0.97), slower speed (< 6.7 mph) and longer distance (≥ 10 miles) group: 0.80 (0.59-1.09), and slower speed (< 6.7 mph) and shorter distance (< 10 miles) group: 0.90 (0.70-1.16). Similar results were found in the joint association of running speed and total amount (cut point at median value of 989 MET-minutes/week) on the risk of developing type 2 diabetes. The combination group with the faster speed and higher total amount of running had the lowest risk (HR 0.58; 95% CI, 0.45-0.74).

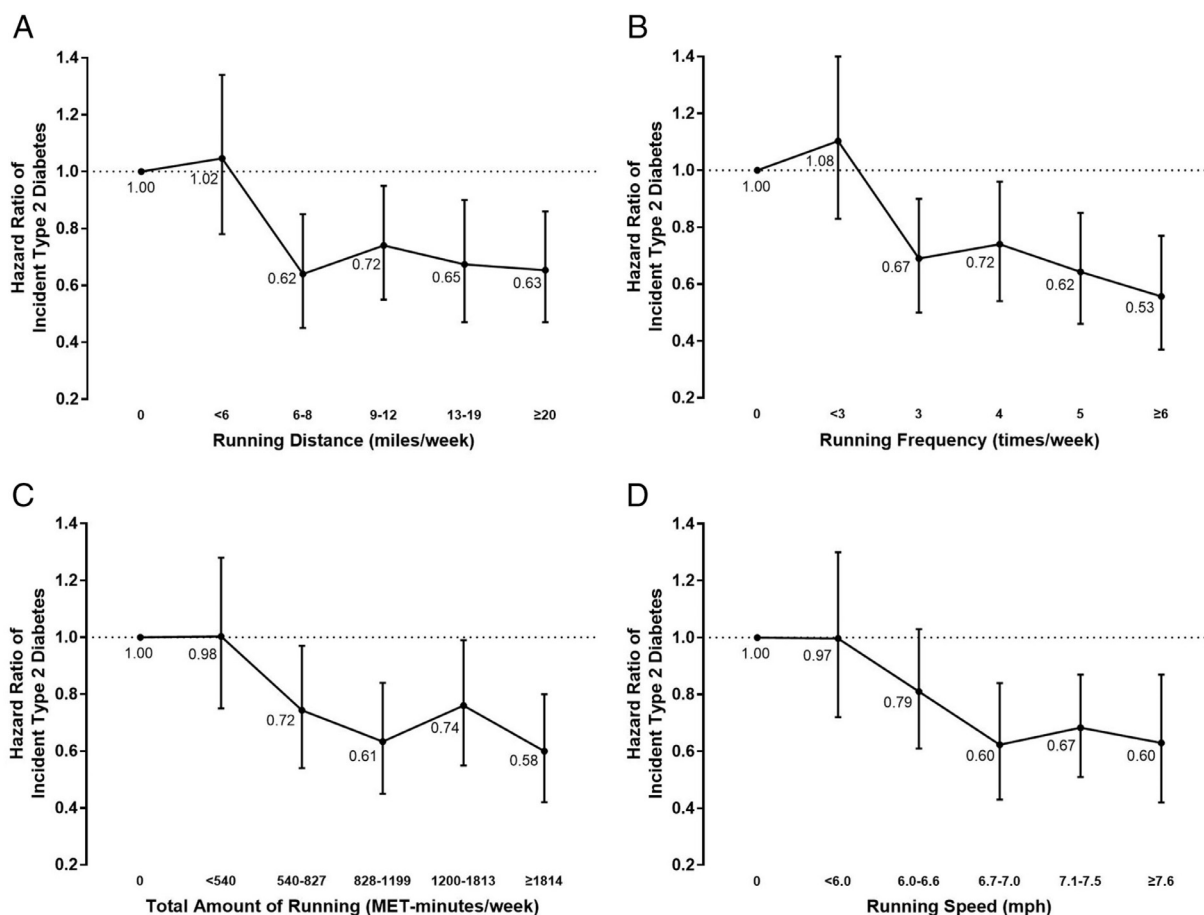
## DISCUSSION

In this large cohort study of adult men and women, runners had a 28% lower risk of developing incident type 2 diabetes compared with nonrunners. Furthermore, consistent linear dose-response associations were observed between various running parameters and incident type 2 diabetes, indicating that more running appears to be better for the prevention of type 2 diabetes.

Because many previous investigations are limited by lack of detailed running information, there are only a few studies focusing on the health benefits of running. Several studies from the National Runners' Health Study, which only included runners, without nonrunners in their analyses, have demonstrated that running is associated with a lower risk of type 2 diabetes prevalence and incidence.<sup>24,25</sup> Our study aligns with previous reports showing the substantial health benefits of running and further indicates a possible protective effect and linear dose-response relationship between leisure-time running and incident type 2 diabetes in adults.

Previous studies with the ACLS dataset have demonstrated that relatively low weekly running doses (< 51 minutes, < 6 miles, 1-2 times, < 506 MET-minutes, or < 6 mph) are associated with reduced risks of all-cause and cardiovascular disease mortality, after adjusting for a similar set of confounders used in our study.<sup>21,26</sup> In the current study, the significant protective effect of running on incident type 2 diabetes arose from weekly running time of 51-80 minutes/week (Quintile 2). However, 73.4% of participants in Quintile 2 participated in running activity < 75 minutes/week (minimum recommendation of vigorous-intensity physical activity), which may suggest that the benefits of running on the prevention of type 2 diabetes could be gained from participating in even less than the recommended amount of vigorous-intensity physical activity.

The protective effect of physical activity on incident type 2 diabetes has been well established by experimental studies and observational studies<sup>4,5,7</sup>; however, most of these studies combined various-intensity physical activity together or focused mainly on moderate-intensity physical activity. To examine whether the benefits in type 2 diabetes prevention came from total physical activity or solely running, we conducted an additional analysis, excluding all participants who reported nonrunning aerobic physical activity. Similar findings were observed with this analysis, indicating that runners, apart from doing other aerobic physical activity, have a reduced risk of type 2 diabetes compared with inactive nonrunners.



**Figure 2** Hazard ratios of incident type 2 diabetes by running distance, frequency, total amount, and speed. Participants were categorized into 6 groups: nonrunners and 5 quintiles of each running distance (A), frequency (B), total amount (C), and speed (D). All hazard ratios were adjusted for baseline age, sex, examination year, BMI, smoking status, heavy alcohol drinking, levels of nonrunning aerobic physical activity, personal history of hypertension, personal history of hypercholesterolemia, ECG abnormality, parental history of diabetes, and baseline fasting glucose. The bars indicate 95% confidence intervals and the dots indicate hazard ratios, which are shown next to the bars. BMI = body mass index; ECG = electrocardiogram; MET = metabolic equivalent.

Several studies suggested that higher levels or greater volumes of physical activity may provide better prevention against type 2 diabetes.<sup>27,28</sup> Moreover, one study found that the benefits of physical activity depend on both amount and intensity, and that higher intensity activities can additionally improve coronary heart disease risk factors beyond total exercise amount (kilometers run per week).<sup>29</sup> These results suggest that, while greater amounts of physical activity appear to provide more benefit, vigorous-intensity physical activity might confer unique health benefits. We also observed similar findings that runners with greater weekly running time at faster speeds, or with greater running amount with higher speeds, showed the lowest risk of developing type 2 diabetes in the 2 joint analyses, respectively, compared with nonrunners.

In our earlier studies, we found that both obesity and low cardiorespiratory fitness have independently contributed to the increased risk of incident type 2 diabetes.<sup>8,30,31</sup> In the current study, runners had a significantly lower BMI and approximately 30% higher cardiorespiratory fitness than

nonrunners. Similar to our running and mortality study,<sup>21</sup> benefits of running on type 2 diabetes disappeared after further adjustment for cardiorespiratory fitness, indicating that cardiorespiratory fitness plays a significant role in the pathway between running and the development of type 2 diabetes.

The common concerns surrounding running are the occurrence of a sudden cardiac event, such as acute myocardial infarction, and musculoskeletal injuries. However, vigorous-intensity physical activity has been associated with decreased risk of incident myocardial infarction and stroke.<sup>32</sup> Additionally, our former study indicated that runners had significantly lower risks of coronary heart disease and stroke mortality, respectively, compared with nonrunners.<sup>21</sup> Regarding musculoskeletal injuries, evidence indicates that long-distance training increases the risk of musculoskeletal injuries;<sup>33</sup> however, many forms of arthritis may actually be lower among chronic runners.<sup>14</sup> Therefore, proper form and education, as well as gradual progression in running amount and speed, are necessary.

Strengths of our study include the collection of detailed running data on various running parameters, comprehensive physical assessments, and controlling of potential confounding factors, including nonrunning aerobic physical activity, in a large sample with a long and comprehensive follow-up. Moreover, due to the extensive and comprehensive baseline physical examination in the clinic, undetected type 2 diabetes cases are less likely to exist in the current study.

There are also several potential limitations of the current study. Because the participants in our study were predominantly non-Hispanic white individuals who were well educated and belonged to middle-to-upper socioeconomic strata, this homogeneity of our sample may limit the generalizability of the results. However, the potential confounding by different races/ethnicities, education, and income levels may be reduced. Although reported vigorous-intensity physical activity is generally more accurate than moderate-intensity physical activity,<sup>34</sup> self-reported running, which is considered as a desirable behavior, is still likely to be over-reported. However, over-reporting typically leads to an underestimation of the beneficial effect of running on type 2 diabetes, suggesting that the effects of running on the risk of type 2 diabetes may be even larger than what we reported when running is objectively measured (eg, accelerometer) in future studies. Our questionnaire did not differentiate between type 2 and type 1 diabetes. However, all diabetes cases in our study were diagnosed after age 30 years, and the National Diabetes Statistics Report identified that more than 90% of adults with diabetes have type 2 diabetes.<sup>35</sup> Thus, there are likely only few participants with type 1 diabetes, which occurs in early age prior to age 30, in our study. Additionally, we did not have sufficient dietary information to include it into our analyses, which is also considered as a significant risk factor for type 2 diabetes. However, we adjusted for BMI in our analyses, as that is affected by diet, specifically, total energy intake.

Our results indicate that runners have a substantially lower risk of developing type 2 diabetes compared with nonrunners after adjusting for potential confounders, including other types of aerobic physical activity. We also found consistent linear dose–response relationships between various running parameters and incident type 2 diabetes. We noted significant benefits of running with lower doses and intensities supporting the prescription of running to prevent type 2 diabetes in adults, in addition to other healthy lifestyle behaviors.

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